

Recurrent chromosome aberrations in fibrous dysplasia of the bone: a report of the CHAMP study group

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Received 22 February 2000; received in revised form 12 April 2000; accepted 14 April 2000

Abstract

The nosologic status of fibrous dysplasia (FD), a well-known and relatively common bone lesion, is controversial. Information collected by the CHromosomes And MorPhology (CHAMP) study group on published and unpublished cases of fibrous dysplasia shows the presence of clonal chromosome changes in at least a proportion of these lesions. The chromosome aberrations found in FD lesions have been quite variable and have included both structural and numerical changes. Two of the three cases investigated at the study group had trisomy 2 as the sole acquired anomaly. Combined with previously published data, +2 and rearrangements involving chromosome band 12p13 have each been detected in 3 of 8 cases with abnormal karyotype of 11 in which chromosomal analysis has been performed, suggesting that FD is a neoplastic lesion rather than a “dysplastic” process, as has been generally believed and as implied by its very name. © 2000 Elsevier Science Inc. All rights reserved.

1. Introduction

In the major textbooks on bone pathology, fibrous dysplasia (FD) is regarded as a non-neoplastic process. It is included in the chapter on “conditions that simulate a bone neoplasm” [1] and it is defined elsewhere as a dysplastic disorder of bone [2]. It is characterized by a broad clinical spectrum, varying from the more frequent solitary (monostotic) asymptomatic lesion to extensive and severe multifo-

cal (polyostotic) lesions. The monostotic variant most commonly affects the ribs, femur, and tibia of older children and young adults. The less frequent polyostotic type may be associated with endocrine abnormalities, skin hyperpigmentation, and soft tissue myxoma (so-called Albright syndrome).

Benign lesions that histologically can be confused with FD are osteofibrous dysplasia of long bones and desmoplastic fibroma. Osteofibrous dysplasia shows bony trabeculae rimmed with osteoblasts embedded in a fibrous stroma. It is an intracortical lesion, whereas FD is a lesion of the medullary cavity. In osteofibrous dysplasia of the long bones, there is maturation from the central part toward the periph-

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ery. Desmoplastic fibroma is histologically indistinguishable from desmoid-type fibromatosis of soft tissue and lacks bone production. Cases of FD with extensive cartilaginous differentiation may be mistaken histologically or radiologically for a benign chondroblastic tumor [3], although the adjacent fibro-osseous component allows this distinction.

The most important differential diagnosis of FD is with low-grade (well differentiated) central osteosarcoma. This may be very difficult because nuclear atypia is minimal in the latter. Recognition is possible because of a permeative growth pattern at the periphery of low-grade central osteosarcoma with infiltration between the surrounding bone trabeculae. This latter feature is well detected on x-rays, whereas FD has an expansive growth pattern with a peripheral sclerotic rim. Rarely, sarcomas can arise in FD and some of them occur in patients who had received radiation therapy (postradiation sarcomas) [4].

Clonal chromosome aberrations have been documented in six of the nine cases of fibrous dysplasia reported [5–9].

Since 1994, the CHAMP (CHromosomes And MorPhology) international study group, composed of cytogeneticists, pathologists, and surgeons has performed systematic studies correlating cytogenetic and clinicopathologic features of a variety of soft tissue tumors [10].

One of the aims of the present CHAMP study was to look for recurrent chromosome aberrations in various benign bone lesions. The present report describes the findings in three cases of FD, and compares these results with previously reported cytogenetic data on this entity.

2. Materials and methods

Three cases of monostotic FD of bone that had been successfully karyotyped in Leuven (Le 369, Le 384) and Lund (LU 497) between 1989 and 1999 were included in the study. One case (Le 369) had been published previously [6], but was reinvestigated by the group to objectively confirm the pathologic diagnosis in the absence of clinical data.

The histopathological diagnosis was reassessed independently by the four pathologists of the group (C.D.M. Fletcher, J. Rosai, G. Tallini, and H. Dorfman) on recut hematoxylin-

and eosin-stained sections from all available blocks of paraffin-embedded tissue, without knowledge of the previous clinical histological or cytogenetic results. In all cases, radiographs were examined as part of the diagnostic procedure.

Karyotypes from short-term cultures were reviewed by the cytogeneticists of the group, without knowledge of the histopathological diagnosis.

3. Results

Clinical data of the cases are summarized in Table 1 (case 2, 7, and 8). All of these were monostotic. On histology, all three lesions showed the typical appearance of fibrous dysplasia: irregular trabeculae of woven bone were embedded in a moderately cellular fibrous matrix. The bony trabeculae had variable and irregular shapes (Fig. 1). Osteoblastic rimming of the trabeculae was characteristically inconspicuous and some of the trabeculae seemed to emerge from the surrounding fibrous background, suggesting a “metaplastic” process. In none of the cases was any associated lesion, such as an aneurysmal bone cyst, detected.

On radiographs, fibrous dysplasia presents as a well-defined osteolytic lesion with benign features, centered within the medulla, and frequently bordered by a shell of reactive sclerosis. Depending on the relative proportion of osseous to fibrous tissue, the lesion can be completely lytic or, most typically, show a relatively high density, the so-called “ground-glass” appearance in at least part of it; especially in bones with small diameter and flat bones, fibrous dysplasia frequently expands the bone. These characteristics were found in all three cases.

Cytogenetically, no structural changes common to all cases were found but trisomy 2 was observed as the sole acquired chromosome abnormality in two of the three cases (Le 384 and Lu 497) (Table 1).

4. Discussion

Fibrous dysplasia is widely regarded as a non-neoplastic process [1,2]. The presence of clonal chromosome aberrations, however, suggests that at least some of the cases hav-

Table 1
Chromosomal abnormalities reported in fibrous dysplasia

Case	Age/Sex	Location	Abnormal karyotype	Reference
1	?/M	?	47,XY,+?8	Tarkkanen et al. [5]
2	19/F	Tibia	46,XX,t(6;11)(q15;p151)	Dal Cin et al. [6] and present report (Le 369)
3	9/F	Sphenoid	46,XX,der(2)?inv(2)(q11q24)del(2)(q31q35)	Dal Cin et al. [6]
4	14/F	Ankle	46,XX,del(3)(q27),add(10)(q22),add(12)(p13)/46,idem,t(3;8)(p21q13),add(10)(q26),der(15)del(15)(q15q22)ins(15;?)(q15;?)/46,idem,-X,+2,t(3;8),add(10),der(15)	Mertens et al. [7]
5	14/F	Fibula	48,XX,+del(12)(p13).ish del(12)(wcp12+,DS12S98-,+mar.ish der(12)(wcp12+,DS12S98×2)	Dal Cin et al. [8]
6	15/M	?	47~49,XY,-2,i(2)(p10),del(4)(p14),+6,+7,+11,add(11)(p15),der(12)(p13q12),-17,-21,+1~3mar	Bridge et al. [9]
7	26/F	Rib	47,XX,+2	Present report (Le 384)
8	39/F	Rib	46,Xc,+2	Present report (Lu 497)

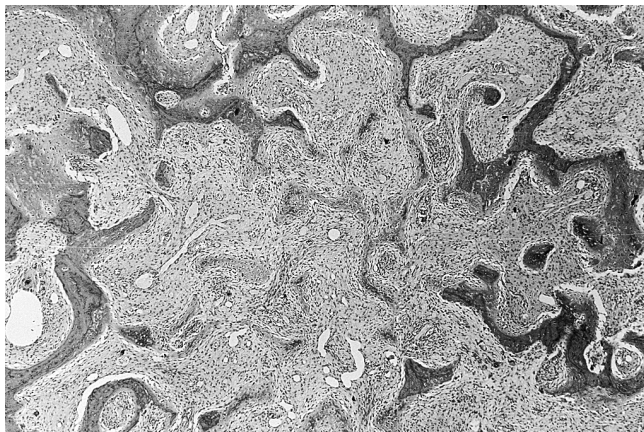


Fig. 1. Low power view, showing the irregular bony trabeculae ("alphabet soup" or "Chinese letters" pattern) in a fibrous background (H & E stain $\times 120$).

ing the clinicopathologic features of this entity are neoplastic in nature [5–9]. The only recurrent changes described thus far in FD have been structural 12p13 aberrations (three cases) and we have added to this trisomy 2 (two cases in this study and one case from the literature [7], (Table 1).

Trisomy 2 has been described previously in other benign fibroblastic proliferations of soft tissues, including proliferative myositis, proliferative fasciitis, and palmar fibromatosis (Dupuytren contracture) [11]. Whether the appearance of trisomy 2 is limited to neoplastic proliferations or may also appear outside a neoplastic context remains to be proven; however, clonal proliferations in mesenchymal mass lesions are generally believed to represent true tumors, although this is not the case in all lymphoid proliferations [12]. Some other fibrous proliferations from which FD needs to be differentiated also were shown to have numerical chromosome changes. Thus, combinations of trisomies for chromosomes 7, 8, 12, 21, and 22 were observed in the few osteofibrous dysplasias that have been investigated cytogenetically [9,13]. Different clonal combinations of trisomies 3 and 5 were also observed in the only case of a desmoplastic fibroma (apparently arising from a FD) thus far reported [14].

In conclusion, the finding of clonal, possibly recurrent chromosome changes in additional cases of FD suggests that this entity is of a neoplastic nature.

Acknowledgments

This text presents research results of the Belgian Programme on Interuniversity Poles of Attraction initiated by

the Belgian State, Prime Minister's Office, Science Policy Programming. The scientific responsibility is assumed by the authors. H. Van den Berghe is supported by F.W.O. (Fund for Scientific Research, Belgium). The work was supported by the Swedish Cancer Society and the Children Cancer Fund of Sweden. The authors thank Rita Logist for clerical assistance.

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